REMARKS

Applicants acknowledge the Examiner's statement that the sequence listing information provided in applicants' October 2, 2000 filing (Paper No. 6) is in compliance with the sequence listing requirement. Applicants also acknowledge the Examiner's statement that, in view of applicants' Statement Deleting Inventors under 37 C.F.R. § 1.63(d) filed June 29, 1999, the inventive entity of the instant application has been amended to delete David W. Thomas and Mihail N. Karpusus.

With respect to the Examiner's assertion regarding the filing date of the instant claims with respect to the recitation of "chronic" and "vasculitis", applicants point out that written description for these phrases is located in priority application United States Serial No. 08/566,238 at page 19, lines 6 to 8, as well as in original claim 60.

The specification has been reviewed for inadvertent typographical errors and identification of all trademarks.

The Title and Abstract

Applicants have amended the title to more particularly reflect the claimed invention. Applicants have also amended the abstract to more particularly describe the claimed invention. None of the amendments to the title or abstract constitutes new matter.

The Drawings

Applicants acknowledge the Examiner's statement that the formal drawings filed in this application comply with 37 C.F.R. § 1.84.

The Claims

Applicants have canceled claims 1 and 102 to 144. This cancellation of claims should not be interpreted as applicants'

acquiescence to any rejection in the outstanding Office Action. Applicants expressly reserve the right to pursue the subject matter of the canceled claims in one or more applications claiming priority herefrom under 35 U.S.C. § 120.

Applicants have added claims 145 to 166 in order to more particularly claim the invention. None of these claim additions constitutes new matter, and the subject matter of each of these claims is fully supported by the disclosure of the instant application, as follows:

Added Claim No.	Support
145	Original claims 50, 55, and 95; Former claims 104, 114, and 124.
146	Original claims 50, 55, and 95; Former claims 114 and 125.
147	Original claims 50, 55, and 95; Former claims 114 and 126.
148	Original claims 38, 50, 55 and 93; Former claim 106.
149	Original claims 39, 41, 43 and 50.
150	Original claims 38, 39, 43 and 50.
151	Former claim 107.
152	Original claim 44; Former claim 108.
153	Original claims 45 to 48; Former claim 109.
154	Original claim 53; Former claim 110.
155	Original claim 69; Former claim 111.
156	Original claim 50; Former claim 115.
157	Former claim 116.
158	Former claim 117.
159	Former claim 120.
160	Former claim 121.

161	Former claim 122.
162	Former claim 123.
163	Former claim 124.
164	Former claim 130.
165	Former claim 133.
166	Former claim 136.

As mentioned above, applicants have canceled former claims 1 and 102 to 144 in order to: (1) more distinctly claim the invention of the instant application and (2) expedite prosecution. To some degree, the outstanding rejections are rendered moot by the claim cancellations and additions herein. Applicants address below the Examiner's remaining contentions.

The Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1, 104 and 106 to 144 stand rejected under 35 U.S.C. § 112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." The Examiner asserts this rejection as follows:

A) Claims 1, 104 and 106 to 144, with respect to "chronic inflammatory autoimmune diseases";

B) Claims 118 and 119, with respect to "[m]ammalian/non-human primate"; and

C) Claims 141 to 144, with respect to "gene therapy vectors", "therapeutic agents", "antigenic pharmaceuticals" and "blood products."

Applicants disagree.

More particularly, with respect to claims 1, 104 and 106 to 144 and "chronic inflammatory autoimmune diseases", the Examiner asserts that "[t]here is insufficient objective evidence that accurately reflects the relative efficacy of the claimed therapeutic strategies to inhibit chronic inflammatory autoimmune diseases, commensurate in scope with the therapeutic methods encompassed by the claimed methods." Specifically, the Examiner cites: Bach (TIPS, 14: 213-216, 1993); Stuber et al. (J. Exp. Med. 183: 693-698, 1996); Gray et al. (J. Exp. Med. 180: 141-155, 1994); Resetkova et al. (Thyroid 6: 267-273); Biacone et al. (Kidney Int. 48: 458-468, 1995); and Larsen et al. (Transplantation 61: 4-9, 1996) for the proposition that: "[i]n contrast to acute conditions, the chronic and complicated nature of the targeted disorders encompassed by the claimed methods are diagnosed only after significant tissue damage has occurred and have an ongoing immune response." The Examiner contends that these documents all report that the administration of a CD40L-CD40 inhibitor -- i.e., anti-gp39 monoclonal antibody (Stuber et al., Resetkova et al., Biacone et al. and Larsen et al.) or sCD40-γ1 (Gray et al.) -- in the face of an ongoing or established immune response has little to no efficacy in treatment or reversal of the established condition. Applicants disagree.

Confirmation of the enablement of CD40L-CD40 inhibitors in an ongoing immune response is provided by the use of humanized monoclonal antibodies as therapeutic agents for the *in vivo* inhibition of CD40L-CD40 mediated allograft rejection in primates, see Kirk et al., Proc. Natl. Acad. Sci., Vol. 94, No. 16, pp. 8789-8794 (1997) - Exhibit B. This study illustrates that applicants' methodology is not unpredictable. Kirk et al. clearly demonstrates that in higher mammals (i.e., primates, in

contrast to the small animal models employed by Stuber et al., Resetkova et al., Biacone et al., Larsen et al. and Gray et al.), the use of the humanized 5c8 monoclonal antibody therapy was effective in blocking CD40L-CD40 interactions, and thereby inhibiting the deleterious immune response which is responsible for the rejection of transplanted organs. More specifically, Kirk et al. teach that 5c8 antibody-treated animals which experienced late, biopsy-proven rejection, successfully restored normal graft function following a repeat course of their induction regimen (Abstract; page 8791, column 2, paragraph 2 and Discussion). This demonstration of suppression of an immune response, which is not an acute, primary-type immune response, supports the methods of the present invention.

Furthermore, viewed as a whole, the disclosure of the present application enables a person skilled in the art, as of applicants' effective filing date, to practice the *in vivo* therapies disclosed therein without undue experimentation. More particularly, applicants disclose: (1) that CD40 ligand on T cells interacts with CD40-bearing cells in such a fashion to result in activation of the CD40-bearing cells (Specification, page 12, lines 4-9 and lines 32-34 and page 13, lines 9-10 and lines 24-27), (2) antibodies which effectively block the interaction of CD40 ligand and CD40 on cells exist (specification, page 13, lines 15-18 and 26-27) and (3) *in vivo* dosage regimes and delivery routes for such antibodies (specification, page 26, lines 25-35 and page 29, lines 5-34).

As demonstrated above, none of the documents cited by the Examiner support the asserted non-enablement of the present invention. In the absence of such evidence to the contrary, the

Examiner has no reason to doubt the objective truth of applicants' asserted operability of the present invention:

> "As a matter of Patent Office practice ... a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented, must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied upon for enabling support... [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." Ex parte Kenaga, 189 USPQ 62, 64 (Pat. Off. Bd. Pat. App. 1975), quoting In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369 (CCPA 1971) (emphasis in original).

Additionally, the Examiner cites two Biogen Press Releases (10/21/99 and 11/2/99), Searchrist (BioWorld Today 10(204); 1,3 - 10/25/99) and an IDEC Pharmaceutical Press Release (4/20/00) in further support of his contention that: "CD40-CD40 ligand antagonists do not appear to inhibit an established or ongoing immune or inflammatory response, encompassed by the claimed methods . . ." The Examiner asserts that: "[i]n view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective antibody-based therapies on inhibiting human transplant rejection, undue experimentation would be required to practice the claimed invention with a reasonable expectation of success, absent a specific and detailed description in applicants'

specification of how to effectively practice the claimed methods and absent a sufficient number of working examples providing evidence which is reasonably predictive that the claimed methods are effective for inhibiting human autoimmunity with 5C8-specific antibodies." Applicants disagree.

In support of the enablement of applicants' invention, true copies of the following Declarations, as filed in co-pending application Serial No. 08/448,130 are filed herewith:

Declaration Under 37 C.F.R. § 1.132 of Akshay Vaishnaw, M.D., Ph.D. and cited documents - (Exhibit C);

Declaration Under 37 C.F.R. § 1.132 of Linda C. Burkly, Ph.D. and cited documents - (Exhibit D); and

Supplemental Declaration Under 37 C.F.R. § 1.132 of Linda C. Burkly, Ph.D. - (Exhibit E).

Applicants point to the above-listed Declarations to rebut the Examiner's concern as to the enablement of the claims in view of the halting of clinical trials involving a humanized 5c8 monoclonal antibody by Biogen, Inc. Specifically, the Vaishnaw Declaration confirms that a person of skill in the art, as of applicants' effective filing date, would reasonably expect that antibodies capable of binding to a protein recognized by monoclonal antibody 5c8, such as monoclonal antibody 5c8 used in the present application, would be useful as agents for inhibiting deleterious immune responses in a human subject.

Dr. Vaishnaw sets forth many parameters which are considered during the pre-clinical stages and clinical trial stages of drug development and emphasizes that these factors may have a complicated interplay. Dr. Vaishnaw is of the opinion that one of ordinary skill in the art, in view of what was known

at the time of filing of this application and in view of all of the information currently available, would look to the use of humanized 5c8 monoclonal antibody for the inhibition of deleterious immune responses. Dr. Vaishnaw is of the opinion that the lack of established clinical protocols, as alleged by the Examiner, has no bearing on whether one of skill in the art at applicants' filing date would be able to practice the claimed methods without undue experimentation because the numerous steps of testing and clinical trials are routine experimentation to obtain such clinical protocols for a particular drug preparation. (See Vaishnaw Declaration, ¶ 8)

In addition, Dr. Burkly states that the voluntary halting of the ANTOVA™ humanized 5c8 antibody clinical trials by Biogen, Inc. would not dissuade a person of skill in the art, as of the effective filing date of this application, from the reasonable belief that a humanized anti-CD40L antibody based on the 5c8 antibody would be useful in inhibiting an unwanted immune response in a human subject. With regard to the investigation being conducted by Biogen, Inc., to more clearly understand the side effects which occurred in the clinical trials, Dr. Burkly states that in view of the results of that investigation to date, one of ordinary skill in the art has insufficient evidence to conclude that the humanized 5c8 monoclonal antibody, itself, and not a component of the delivery vehicle, is the causative agent of the observed adverse events. Dr. Burkly makes clear that the causative agent has not yet been identified. (See Burkly Declaration, ¶ 10; see also Vaishnaw Declaration ¶ 10 and Supplemental Burkly Declaration ¶ 3)

The standards of the Federal Drug Administration which are required to be met by an applicant for drug approval are not the standards for patentability before the United States Patent and Trademark Office. The M.P.E.P. (7th ED. 2000) at § 2164.05, page 2100-34, states that "considerations made by the FDA for approving clinical trials are different from those made by the PTO in determining whether a claim is enabled." In addition, see Scott v. Finney, 34 F.3d 1058, 1063, 32 USPQ 1115, 1120 (Fed. Cir. 1994) ("Testing for full safety and effectiveness of a prosthetic device is more properly left to the [FDA].")

Applicants' specification, in combination with what was known to one of skill in the art as of its effective filing date, would have enabled the skilled person to carry out the presently claimed invention without undue experimentation.

It is well established that "enablement requires that the specification teaches those in the art to make and use the invention without undue experimentation." In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1408 (Fed. Cir. 1988). As a matter of law, the enablement requirement is met even if some routine experimentation is necessary in order to practice the invention.

The Examiner also asserts the § 112, first paragraph rejection against claims 118 and 119 for the recitation of "[m]ammal/non-human primate". In particular, the Examiner states that: "[a]pplicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies the 5C8/CD40L specificity in the breadth of mammalian and non-human species recited in claims 118-119." Applicants have canceled the recitation of "mammal" and "non-human primate" from the claims in

order to expedite allowance of this application, and accordingly, this rejection is moot.

The Examiner further asserts the § 112, first paragraph rejection against claims 141 to 144. The Examiner contends that the specification contains insufficient guidance and direction for the concepts of "gene therapy vectors", "therapeutic agents", "antigenic pharmaceuticals" and "blood products." According to the Examiner: ". . . undue experimentation would be required of one skilled in the art to practice the claimed methods to "gene therapy vectors", "therapeutic agents", "antigenic pharmaceuticals" and "blood products"[.] commensurate in scope with the claimed invention using the teaching of the specification."

The amended claims do not recite "gene therapy vectors", "therapeutic agents", "antigenic pharmaceuticals" or "blood products", and as such, the § 112, first paragraph rejection is rendered moot.

Finally, with respect to the § 112, first paragraph rejection, the Examiner points to Luqmani et al. (Scand. J. Rheumatol. 29: 211-15, 2000) for the proposition that: "specific therapies are available in some types of vasculitis but [in] the majority of the cases, non-specific interference with the immune system is most appropriate."

Applicants point out that, contrary to the Examiner's interpretation, Luqmani et al. suggests that: "[t]here is a current interest in more specific interference with the immune system in systemic vasculitis". Luqmani et al. also refers to "the successful use of polyclonal and monoclonal anti-T cell antibodies" -- see page 312, second column, last 3 paragraphs.

Consistent with Luqmani et al., the methods of the instant application utilize an antibody which "specifically" targets the cells responsible for inducing the inflammatory component of vasculitis. According to one embodiment, applicants' invention directly inhibits deleterious immune responses by inhibiting the transmigration of inflammatory cells across a barrier of endothelial cells in patients suffering from vasculitis -- see, in this respect, claim 151. As such, the Examiner's reliance on Luqmani et al. is misplaced, and the rejection under 35 U.S.C. § 112, first paragraph should be withdrawn.

Applicants acknowledge the Examiner's statement that the 5c8 antibody is enabled, based on the availability of the 5c8 antibody produced by the hybridoma designated as ATCC HB 10916, as evidenced by United States patent 5,474,771.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1, 104 and 106 to 144 stand rejected under 35 U.S.C. § 112, second paragraph, as being "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant[s] regards as the invention essentially for the reasons set forth in the previous Office Actions (Paper Nos. 22/25)." More particularly, the Examiner asserts that claims 1, 104 and 106 to 144 are indefinite in the recitation of "and a portion thereof" because it is not clear which portion is being referred to and the metes and bounds are not defined.

The added claims do not longer recite the phrase "and a portion thereof" -- see, in this respect, claims 145 to 147. Instead, the claims specify that the anti-CD40L compound is a

CD40L-specific antibody, Fab, F(ab)'2 or a single chain antibody, as illustrated in the specification -- see page 26, lines 1 to 7 of the specification.

These phrases are not indefinite, particularly in view of the fact that the recited structures are further defined with respect to their function of "binding specifically to an antigen specifically bound by monoclonal antibody 5c8, produced by the hybridoma having ATCC Accession No. HB 10916" -- see, in this respect, claims 145 to 147 as added herein.

The Examiner further contends that "[e]ven in the claims reciting, 'comprises a Fab ...' the recitation of 'comprises' opens the claim to include other elements not clearly defined or disclosed."

Applicants point out that sufficient guidance is provided in the specification and sufficient elements are recited in the claims to render definite the recitation of "comprises". For example, the characteristics defined and disclosed in the instant application include: (1) an antibody, Fab, F(ab)'2 or a single chain antibody, and (2) the ability to bind specifically to an antigen specifically bound by monoclonal antibody 5c8, produced by the hybridoma having ATCC Accession No. HB 10916. Based on these two characteristics one of skill in the art, would easily be able to identify the subject matter of the applicants' invention as claimed. As such the metes and bounds of the invention are not indefinite and the § 112, second paragraph rejection should be withdrawn.

The Examiner further asserts the § 112, second paragraph rejection against claims 141 to 144, as being indefinite in the recitation of "administered" with a gene

therapy vector or a therapeutic agent because the intention of the claim in the context of "treating vasculitis" is unclear.

The amended claims do not recite the use of "administered" with a gene therapy vectors or a therapeutic agent and as such, the § 112, second paragraph rejection is rendered moot.

The Rejection Under 35 U.S.C. § 102(e)

Claims 104 and 106 to 144 stand rejected under 35 U.S.C. § 102(e) as being "anticipated by" Noelle et al. (United States patent 5,683,696). More specifically, the Examiner asserts that Noelle et al. "teaches methods of inhibiting tissue/organ rejection with CD40L-specific antibodies (e.g. gp39-specific and 5C8-specific antibodies), including the use of recombinant antibodies and fragments ... in conventional methods including various dosages and modes of administration ..." Additionally, the Examiner contends that Noelle et al.'s use of antigen presenting cells parallels the claimed blood products and antigenic pharmaceuticals. Finally, the Examiner asserts that Noelle et al. teaches the ability of CD40L-specific antibodies to inhibit T cell responses and CD40L interactions with other cell types including B cells and endothelial cells. Applicants traverse.

Applicants have obviated this rejection by more distinctly claiming their invention. Specifically, the amended claims are not directed to blood products and antigenic pharmaceuticals. Furthermore, Noelle et al. fails to teach or disclose each and every element of the methods of applicants' claims. In particular, Noelle et al. fails to teach the specific

dosages and administration regimens and modalities, particularly with respect to the claimed treatment of vasculitis, -- see, in this respect, added claims 144 to 147 and claims 160 to 166. Accordingly, these § 102(e) rejections should be withdrawn.

Claims 1 and 104 to 138 stand rejected under 35 U.S.C. § 102(e) over Black et al. (United States patent 6,001,358). More particularly, the Examiner asserts that Black et al. "teaches methods of inhibiting tissue/organ rejection and GVHD [(graft-versus-host disease)] ... and vasculitis ... with CD40L-specific antibodies ... including the use of recombinant antibodies and fragments ... in conventional methods including various dosages and modes of administration ..." Additionally, the Examiner contends that "given the nature of the graft rejection including transplantation and GVHD and that, the graft microvascular endothelia express an inflamed phenotype associated with wound healing and the repair of tissue damage due to mechanical trauma; inhibiting vasculitis would be inherent in the referenced methods."

Applicants have obviated this rejection by more distinctly claiming their invention. Black et al. fails to disclose each and every element of applicants' added claims. In particular, Black et al. fails to teach the specific dosages and administration regimens and modalities of the applicants' methods as claimed, particularly with respect to the treatment of vasculitis -- see, in this respect, added claims 144 to 147 and claims 160 to 166. Accordingly the § 102(e) rejection should be withdrawn.

The Rejection Under 35 U.S.C. § 103

Claims 1, 104 and 106 to 144 stand rejected under 35 U.S.C. § 103 as being "unpatentable over" Noelle et al. (United States patent 5,683,696) and/or Black et al. (United States patent 6,001,358), in view of Lederman et al. (WO 93/09812, Morgan et al. (Transplantation 55: 919-923, 1993) and Haug et al. (Transplantation 55: 766-773, 1993). In addition to the asserted disclosures of Noelle et al. and Black et al., the Examiner contends that: Lederman et al. teaches the inhibition of various immune cell interactions associated with 5c8-specific antibodies, including recombinant antibodies and methods for screening said antibodies; Morgan et al. teaches the role of T cells in graft rejection including after transplantation; and Haug et al. teaches that inhibition of leukocytes with antibody therapy could be useful in controlling allograft rejection and limiting reperfusion injury, as well as that the use of anti-ICAM-1 antibodies to inhibit both the stimulatory and effector stages of T cell mediated graft rejection.

As stated above, neither Noelle et al. nor Black et al. teaches or suggests the claimed specific dosages and administration regimens of applicants' claimed methods, particularly with respect to the treatment of vasculitis. To that end, the disclosure of Lederman et al., Morgan et al., or Haug et al. either separately or in combination, does not teach or suggest such dosages or regimens. Furthermore, nothing in Noelle et al., Black et al., Lederman et al., Morgan et al., or Haug et al. either separately or in combination, would have led a person of skill in the art at the effective filing date of this application to employ the specific administration regimens or

dosages of CD40L-specific antibodies claimed herein for the treatment of vasculitis.

Applicants disagree the Examiner's assertion that: "[o]ne of ordinary skill in the art at the time the invention was made would have been motivated to select the ability of CD40L-specific antibodies to inhibit graft rejection and, in turn, to expect or to apply such modalities to inhibit vasculitis."

More particularly, the present invention, as claimed herein, relates to the treatment of vasculitis in human patients at specific dosages -- see, in this respect, claims 144 to 147, and with specific regimens and delivery modalities -- see, in this respect, claims 160 to 166. None of the documents cited by the Examiner, either alone or in combination, teaches these specific dosages, specific regimens or specific modalities for the treatment of humans suffering from vasculitis. At most, those documents would constitute a "suggestion to try". However, "obvious to try" is not the standard for patentability:

> In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

Claims 141 to 144 stand further rejected under 35 U.S.C. § 103 over Noelle et al., Black et al., Lederman et al., Morgan et al. and Haug et al., in further view of Humphries et al. (United States patent No. 5,804,177). In particular, the Examiner contends that Noelle et al., Black et al., Lederman et al., Morgan et al. and Haug et al., differ from the claimed

methods by not disclosing gene therapy vectors. The Examiner further asserts that Humphries et al. teaches the use of recombinant vectors to express MHC antibodies to induce immunological tolerance or non-responsiveness. The Examiner asserts that: "[g]iven the breadth of gene therapy vectors and antigenic pharmaceuticals, the referenced vectors employed in methods to induce immunological non-responsiveness as taught by Noelle et al. would be encompassed by the claimed methods."

The amended claims do not recite the use of "gene therapy vectors" and as such, the § 103 rejection based on the above-cited documents in view of Humphries et al. is rendered moot.

Applicants request that the Examiner consider the foregoing amendments and remarks, and withdraw the claim rejections.

Respectfully submitted,

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I Hereby Certify that this Correspondence is being Deposited with the U.S. Postal Service as First Class Mail in an Envelope Addressed to: ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231 on

June 13, 2001

Claudia J. Gaintil

Signature of Person Signing

APPENDIX

IN THE TITLE

Please amend the title to read as follows:

THERAPEUTIC APPLICATIONS FOR THE ANTI-T-BAM (CD40L) MONOCLONAL ANTIBODY 5C8 IN THE TREATMENT OF VASCULITIS [CHRONIC INFLAMMATORY DISEASE]

IN THE ABSTRACT

Please amend the abstract to read as follows:

Activation of cells bearing CD40 on their surface by CD40 ligand is inhibited by contacting the cells with an agent capable of inhibiting interaction between CD40 ligand and the cells, in an amount effective to inhibit activation of the cells. Activation of cells bearing CD40 on their surface by CD40 ligand in a subject is inhibited by administering to the subject an agent capable of inhibiting the interaction between CD40 ligand and the cells, in an amount effective to inhibit activation of the cells. Conditions dependent on CD40 ligand-induced activation of CD40-bearing cells are treated, in particular vasculitis.

IN THE CLAIMS

145. (added) A method for treating vasculitis in a human comprising the step of administering to said human, other than a transplant recipient, an antibody, Fab, F(ab)'2 or a single chain antibody, which binds specifically to an antigen specifically bound by monoclonal antibody 5c8, produced by the hybridoma having ATCC Accession No. HB 10916, wherein said antibody, Fab, F(ab)'2 or a single chain

antibody, is administered to said human at a dosage range of between about 0.01 and 200 mg/kg body weight of said human.

146. (added) A method for treating vasculitis in a human comprising the step of administering to said human, other than a transplant recipient, an antibody, Fab, F(ab)'2 or a single chain antibody, which binds specifically to an antigen specifically bound by monoclonal antibody 5c8, produced by the hybridoma having ATCC Accession No. HB 10916, wherein said antibody, Fab, F(ab)'2 or a single chain antibody, is administered to said human at a dosage range of between about 0.01 and 50 mg/kg body weight of said human.

147. (added) A method for treating vasculitis in a human comprising the step of administering to said human, other than a transplant recipient, an antibody, Fab, F(ab)'2 or a single chain antibody, which binds specifically to an antigen specifically bound by monoclonal antibody 5c8, produced by the hybridoma having ATCC Accession No. HB 10916, wherein said antibody, Fab, F(ab)'2 or a single chain antibody, is administered to said human at a dosage range of between about 1 and 30 mg/kg body weight of said human.

148. (added) The method according to any one of claims 145 to 147, wherein said antibody, Fab, F(ab)'2 or a single chain antibody, specifically inhibits cell activation by CD40 ligand of CD40-bearing cells which are involved in an inflammatory response.

149. (added) The method according to any one of claims 145 to 147, wherein said antibody, Fab, F(ab)'2 or a single chain antibody, inhibits binding of CD40 ligand to CD40 on the surface of endothelial cells, fibroblasts, epithelial

cells, T cells, basophils, macrophages or dendritic cells in said human.

150. (added) The method according to any one of claims 145 to 147, wherein said antibody, Fab, F(ab)'2 or a single chain antibody, inhibits the interaction between CD40 ligand and CD40 on the surface of endothelial cells, fibroblasts, epithelial cells, T cells, basophils, macrophages or dendritic cells in said human.

151. (added) The method according to any one of claims 145 to 147, wherein said antibody, Fab, F(ab)'2 or single chain antibody is effective to inhibit transmigration of inflammatory cells across a barrier of endothelial cells in said human.

152. (added) The method according to any one of claims 145 to 147, wherein said antibody is a monoclonal antibody or a polyclonal antibody.

153. (added) The method according to any one of claims 145 to 147, wherein said antibody is selected from the group consisting of: chimeric antibodies, primatized antibodies, humanized antibodies and antibodies which include a CDR region from a first human and an antibody scaffold from a second human.

154. (added) The method according to any one of claims 145 to 147, wherein said antibody is monoclonal antibody 5c8 which is produced by the hybridoma having ATCC Accession No. HB 10916.

155. (added) The method according to any one of claims 145 to 147, wherein said antibody is a humanized monoclonal

antibody 5c8 or a primatized monoclonal antibody 5c8.

156. (added) The method according to any one of claims 145 to 147, wherein said antibody, Fab, F(ab)'2 or single chain antibody is selected by a screening method, which comprises the steps of:

(a) isolating a sample of CD40-bearing cells which are involved in an inflammatory response;

(b) culturing said sample under conditions permitting activation of the CD40-bearing cells;

(c) contacting said sample with:

(i) cells expressing a protein which is specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 10916, or

(ii) a protein which is specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 10916,

under conditions which permit activation of said CD40-bearing cells;

(d) contacting said sample with an antibody, Fab, F(ab)'2 or a single chain antibody, under conditions which permit said antibody, Fab,

F(ab)'2 or single chain antibody to inhibit activation of said CD40-bearing cells; and

(e) determining whether the (i) cells expressing a protein which is specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 10916, or (ii) protein which is specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 10916, activate the CD40-bearing cells in the presence of the antibody, Fab, F(ab)'2 or single chain antibody.

157. (added) The method according to claim 156, wherein said sample of CD40-bearing cells is isolated from a tissue.

159. (added) The method according to claim 156, wherein said sample of CD40-bearing cells is selected from the group consisting of: cell lines in culture, cells isolated from an animal and cells isolated from a body fluid.

158. (added) The method according to any one of claims 145 to 147, wherein said antibody, Fab, F(ab)'2 or single chain antibody is administered to said human by a parenteral route.

160. (added) The method according to claim 159, wherein said parenteral route is selected from the group consisting of: intravenous, intravascular, intraarterial,

subcutaneous, intramuscular, intratumor, intraperitoneal, intraventricular, intraepidural, oral, nasal, opthalmic, rectal, topical and inhalation routes.

161. (added) The method according to any one of claims 145 to 147, wherein said antibody, Fab, F(ab)'2 or single chain antibody is administered to said human by sustained release administration.

162. (added) The method according to claim 161, wherein said sustained release administration comprises depot injection of an erodible implant.

163. (added) The method according to any one of claims 145 to 147, wherein said antibody, Fab, F(ab)'2 or single chain antibody is administered to said human at intervals ranging from each day to every other month.

164. (added) The method according to any one of claims 145 to 147, wherein said antibody, Fab, F(ab)'2 or single chain antibody is administered to said human daily for the first three days of treatment, after which the antibody, Fab, F(ab)'2 or single chain antibody is administered every 3 weeks, with each administration being intravenously at 5 or 10 mg/kg body weight of said human.

165. (added) The method according to any one of claims 145 to 147, wherein said antibody, Fab, F(ab)'2 or single chain antibody is administered to said human daily intravenously at a dosage of 5 mg/kg body weight of said human for the first three days of treatment, after which the antibody, Fab, F(ab)'2 or single chain antibody is administered subcutaneously or intramuscularly every week at a dosage of 10 mg/kg body weight of said human.

166. (added) The method according to any one of claims 145 to 147, wherein a single dose of said antibody, Fab, F(ab)'2 or single chain antibody is administered to said human parenterally at 20 mg/kg body weight of said human, followed by administration of the antibody, Fab, F(ab)'2 or single chain antibody subcutaneously or intramuscularly every week at a dosage of 10 mg/kg body weight of said human.